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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/348,354	07/07/1999	MENZO HAVENGA	4123US	5117

7590 09/20/2002

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EXAMINER

LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
1636	30

DATE MAILED: 09/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application N .	Applicant(s)
	09/348,354	HAVENGA ET AL.
	Examiner	Art Unit
	Gerald G Leffers Jr.	1636

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 21 August 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) The period for reply expires 3 months from the mailing date of the final rejection.
- b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. The proposed amendment(s) will not be entered because:
 - (a) they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) they raise the issue of new matter (see Note below);
 - (c) they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet.

3. Applicant's reply has overcome the following rejection(s): _____.
4. Newly proposed or amended claim(s) ____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. For purposes of Appeal, the proposed amendment(s) a) will not be entered or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 2,3,9-11 and 33-48.

Claim(s) withdrawn from consideration: 13-32.

8. The proposed drawing correction filed on ____ is a) approved or b) disapproved by the Examiner.

9. Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.

10. Other: See Continuation Sheet

Advisory Action Attachment

Continuation of 2. NOTE: The amendment of the claims to delete the phrase "at its N-terminus" broadens the scope of the claims and raises additional art issues.

Continuation of 5. does NOT place the application in condition for allowance because: of the following reasons. First, those arguments directed towards the amended claims are moot in that the amendment to the claims has not been entered (see above). The response also argues that the rejection under 35 USC 103(a) of claims as being obvious over Crystal et al in view of Wickham et al is not proper on at least two grounds. The response argues that the proposed combination of references does not teach all the claim limitations (i.e. that the second serotype adenoviral fiber is obtained from Ad11 , Ad14, etc.). The response further argues lack of motivation to combine the reference teachings. These arguments are not persuasive for several reasons.

With regard to the allegation that not all of the limitations are taught by the combined references, the response argues that for Crystal et al the "express" teachings are only directed towards fiber replacement (e.g. example 2) such that a chimeric capsid results, rather than a chimeric fiber. Also, the response argues that the Wickham et al teachings with respect to fiber chimeras, wherein the amino terminal domain is retained and the tropism domain switched, are limited to Ad5/Ad2 or Ad5/Ad3 and thus does not offset the deficiencies of the Crystal et al reference. Crystal et al clearly contemplate embodiments where the second adenoviral fiber is obtained from those adenoviral serotypes recited in the rejected claims. For example, the specification teaches "A "coat protein" according to the invention is either an adenoviral penton base protein, an adenoviral hexon protein, or an adenoviral fiber protein." Also, "Optimally,

however, the adenovirus coat protein is that of a Group B or C adenovirus and, preferably, is that of Ad1, Ad2, Ad3, Ad5, Ad6, Ad7, Ad11, Ad12, Ad14, Ad16, Ad21, Ad34, Ad35, Ad40, Ad41, or Ad48." (column 4, lines 32-41). The spec also teaches "For instance, preferably a region of an Ad2 coat protein can be replaced with the corresponding region of an Ad5 or Ad7 coat protein (or any other serotype of adenovirus as described above), and vice versa." (column 10, lines 41-51). The spec also teaches "Fiber protein sequences and methods of modifying fiber protein are known to those skilled in the art (see, e.g., Xia et al., Novelli et al., *Virology* 185, 365-376 (1991)). The fiber manipulations can be carried out in the absence of, or along with, modifications to the adenovirus hexon protein. In particular, preferably the fiber protein can be replaced in its entirety, or in part, with sequences of a fiber protein from a different serotype of adenovirus." (column 11, lines 51-58). Thus, Crystal et al does teach the construction of adenoviral vectors comprising chimeric hexon and chimeric fiber proteins and wherein the chimeric fiber can be derived from adenoviral capsids of the serotypes recited in the rejected claims.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Crystal et al make clear that it is possible to construct adenoviral vector having chimeric hexon proteins and chimeric fiber proteins for the purpose of constructing a vector that

is not as antigenic as a “wildtype” adenoviral vector lacking the nonnative sequences in the adenoviral hexon or fiber. Wickham et al make clear that it is within the skill of the art for one to construct and use an adenoviral gene transfer vector that comprises a chimeric fiber protein such that the tropism of the adenoviral vector is altered to a desired cell type displaying a particular receptor that binds the chimeric fiber. The adenoviral vectors taught by Crystal et al and Wickham et al are both involved in the transfer of a desired gene to a cell of a desired trait and are analogous in function. One of ordinary skill in the art and aware of the teachings of Crystal et al and Wickham et al would readily recognize the advantages of having an adenoviral gene transfer vector that has 1) decreased antigenicity (as taught by Crystal et al) and 2) tropism for a desired cell type (as taught by Wickham et al). Absent any evidence to the contrary, and in contradiction to the assertion that the rational for combination of the two references is merely an “obvious-to-try” motivation, there would have been a reasonable expectation of combining the teachings of Crystal et al and Wickham et al to construct and use an adenoviral vector having decreased antigenicity (e.g. an altered hexon protein as taught by Crystal et al) and altered tropism (e.g. an altered receptor binding domain as taught by Wickham et al). Applicants have provided no indication as to why such an adenoviral vector could not be constructed and why it would not work.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

AAZ
ggl
September 16, 2002

DAVID GUZO
PRIMARY EXAMINER
David Guzo